PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/US2005/003766	International filing date *(day/month/year)* 04.02.2005
Priority date *(day/month/year)* 05.02.2004	
International Patent Classification (IPC) or both national classification and IPC INV. C07K14/57 G01N33/68 A61K38/21 A61K39/00 C12N15/23 C12N15/63	
Applicant THE ARIZONA BOARD OF REGENTS, A BODY CORPORATE...	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/003766

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 5-13,33-37 (completely), 14-32 (partially), and 18-32 with respect to IA

because:

☒ the said international application, or the said claims Nos. 18-32 with respect to IA relate to the following subject matter which does not require an international preliminary examination *(specify)*:
see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 5-13,33-37 (completely) and 14-32 (partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/003766

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-4 (completely) and 14-32 (partially)

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-4
	No:	Claims	1,14-32
Inventive step (IS)	Yes:	Claims	2-4
	No:	Claims	1,14-32
Industrial applicability (IA)	Yes:	Claims	1-4,14-17
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 18-32 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item IV
Lack of unity of invention

The problem to be solved by the present application resides in the provision of compounds for treatment of diseases by stimulating immune system activity, including infection, tumor, bone diseases and pain.
As a solution, polypeptide mimetics of GalNAc are provided.
The technical feature in the sense of Rule 13.2 PCT which a priori could unify different solutions is the entity of being a polypeptide mimetic of GalNAc.
However, such a solution has already been proposed in the prior art, see e.g. the international patent application WO 02/058589 disclosing a DBP (vitamin D binding protein) peptide comprising an N-acetyl galactosamine for use in promoting bone deposition (see claims 1-3,5,9-11, pages 4,5 and Figure 1), or the international patent application WO 00/31130 disclosing the peptide AETVESCLAKSH corresponding to SEQ ID NO: 23 of the present application for use in treatment of HCV infection (see SEQ ID NO:17, page 5, claims 1,23).
The problem to be solved may therefore be considered to be the provision of further polypeptide mimetics of GalNAc.
However, a structural relationship among the polypeptides of the different subjects which could fulfil the role of a "special technical feature" in the sense of Rule 13.2 PCT is missing.

Unity of invention is also lacking between subjects 1 to 5 on the one hand and subject 6 on the other hand.
The technical feature of independent claim 33 resides in the step of observing the effect of

the candidate compounds on ligand binding in a screening assay. Neither the same nor a corresponding special technical feature is present in any of the compounds of claims 1 to 13. No manufacturing relationship exists between the screening method and the claimed compounds. Further, the screening method of independent claim 33 is not a method of using claimed compounds. In the absence of any teaching as to the structure required for a compound to act as a receptor antagonist, there is no single general concept in the sense of Rule 13.1 PCT that links the method to the claimed compounds.

As there are no other special technical features, the present application is found to lack unity of invention, giving rise to the 6 subjects as defined in the "Invitation to pay additional fees".
Since performing a search for all subjects would involve considerable supplementary search effort, a search was performed for the first subject only.

Re Item V
Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: US-B1-6 551 795 (RUBENFIELD MARC J ET AL) 22 April 2003 (2003-04-22)
D2: WO 02/058589 A (NORTHEASTERN OHIO UNIVERSITIES COLLEGE OF MEDICINE; SCHNEIDER, GARY, B) 1 August 2002 (2002-08-01)

Novelty

The document D1 discloses a polypeptide comprising the sequence QGSQRLSATAR corresponding to formula 1 of the present application (see SEQ ID NO:27024, aa 310-320). The polypeptide is useful for treatment of pathological conditions resulting from bacterial infection.
Therefore, the subject-matter of claims 1 and 14-32 does not meet the requirements of Article 33(2) PCT.

Inventive step

The document D2 is regarded as being the closest prior art to the subject-matter of claims 2 to 4, and shows (the references in parentheses applying to this document) a DBP (vitamin D binding protein) peptide comprising an N-acetyl galactosamine for use in promoting bone deposition (see claims 1-3,5,9-11, pages 4,5 and Figure 1).
The subject-matter of claims 2 to 4 differs from this known D2 in that different compounds are provided.

The subject-matter of claims 2 to 4 is therefore new (Article 33(2) PCT).

The problem to be solved by the present invention may be regarded as providing further compounds for stimulating immune system activity in a subject to treat diseases, including bone disorders, infections and tumors.
The solution to this problem proposed in claims 2 to 4 of the present application is considered as involving an inventive step (Article 33(3) PCT), since none of the cited documents teaches or suggests the use of compounds according to claims 2 to 4 for stimulating immune system activity in a subject.

The same reasoning applies mutatis mutandis to claims 14-32, in so far as the compounds according to claims 2 to 4 are concerned.

Industrial applicability

For the assessment of the present claims 18 to 32 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.